



Clinical trial results:

A multicentre, double-blind, randomised, placebo-controlled phase II trial with a 3-week treatment period to assess the efficacy, safety and tolerability of add-on treatment with Ketamine hydrochloride prolonged release tablets (KET01, 120 mg or 240 mg once daily) in outpatients with treatment resistant depression

Summary

EudraCT number	2021-004927-34
Trial protocol	DE CZ PL
Global end of trial date	10 May 2023

Results information

Result version number	v1 (current)
This version publication date	24 May 2024
First version publication date	24 May 2024

Trial information

Trial identification

Sponsor protocol code	KET01-02
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ketabon GmbH
Sponsor organisation address	Wilhelm-Wagenfeld-Straße 20, München, Germany, 80807
Public contact	Hans Eriksson, MD, PhD, MBA, Sponsor's Medical Expert, 0049 15172515268, hans.eriksson@hmnc-brainhealth.com
Scientific contact	Hans Eriksson, MD, PhD, MBA, Sponsor's Medical Expert, 0049 15172515268, hans.eriksson@hmnc-brainhealth.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 April 2023
Global end of trial reached?	Yes
Global end of trial date	10 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the efficacy of KET01 (120 mg or 240 mg) administered once daily (OD) as add-on therapy to standard treatment compared to placebo with respect to improvement of depressive symptoms assessed by change in Montgomery-Åsberg Depression Rating Scale (MADRS) total score in subjects with major depressive disorder (MDD), fulfilling criteria for treatment-resistant depression (TRD).

Protection of trial subjects:

This trial was performed in compliance with Good Clinical Practices (GCP) and applicable regulatory requirements, including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 May 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 53
Country: Number of subjects enrolled	Czechia: 52
Country: Number of subjects enrolled	Poland: 62
Worldwide total number of subjects	167
EEA total number of subjects	167

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	166
From 65 to 84 years	1

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

This exploratory trial was performed from May 2022 to May 2023 at 29 sites in Czech Republic, Germany and Poland. 167 subjects enrolled in the trial

Pre-assignment

Screening details:

Subjects who met all the inclusion criteria and none of the exclusion criteria. Of the 167 subjects enrolled in the trial, 45 were screening failures and 122 were kept to be randomised to receive either KET01 240 mg, KET01 120 mg or placebo at Treatment Period - Visit 2b.

Pre-assignment period milestones

Number of subjects started	167
Number of subjects completed	122

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Adverse event, non-fatal: 1
Reason: Number of subjects	Consent withdrawn by subject: 1
Reason: Number of subjects	Ineligibility/development of 1/mult. excl. crit.: 42
Reason: Number of subjects	Lost to follow-up: 1

Period 1

Period 1 title	Baseline - Visit 2a
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

At this visit, where baseline values are evaluated, there was still no allocation to treatment done. This period and its arms are defined due to technical issues since validator expects a postassignment period marked for baseline and expects definition of arms for a postassignment period.

Arms

Are arms mutually exclusive?	Yes
Arm title	Baseline - KET01-240

Arm description:

Defined due to technical issues: Subjects that were randomised to KET01-240 at Visit 2b. Visit 2a is part of preassignment screening period

Arm type	Active comparator
Investigational medicinal product name	None
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

Defined due to technical issues: Subjects that were randomised to KET01-240 at Visit 2b. Visit 2a is part of preassignment screening period

Arm title	Baseline - KET01-120
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Arm description:

Defined due to technical issues: Subjects that were randomised to KET01-120 at Visit 2b. Visit 2a is part of preassignment screening period

Arm type	Active comparator
Investigational medicinal product name	None
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

Defined due to technical issues: Subjects that were randomised to KET01-120 at Visit 2b. Visit 2a is part of preassignment screening period

Arm title	Baseline - Placebo
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Arm description:

Defined due to technical issues: Subjects that were randomised to Placebo at Visit 2b. Visit 2a is part of preassignment screening period

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

Defined due to technical issues: Subjects that were randomised to Placebo at Visit 2b. Visit 2a is part of preassignment screening period

Number of subjects in period 1^[1]	Baseline - KET01-240	Baseline - KET01-120	Baseline - Placebo
Started	40	42	40
Completed	40	42	40

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Number of subjects in the baseline period are defined as subjects who met all the inclusion criteria and none of the exclusion criteria. Of the 167 subjects enrolled in the trial, 45 were screening failures and 122 were kept to be randomised to receive either KET01 240 mg, KET01 120 mg or placebo at Treatment Period.

Period 2

Period 2 title	Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
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Arm title	Treatment - KET01-240
Arm description: KET01 240 mg once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial	
Arm type	Active comparator
Investigational medicinal product name	Ketamine hydrochloride (HCl)
Investigational medicinal product code	KET01
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

KET01 tablets 40 mg (pink), KET01 tablets 80 mg (white) and Placebo tablets matching KET01 tablets 40 mg (pink) and 80 mg (white) for oral administration.
Subjects took a total daily dose of 240 mg ketamine hydrochloride by 2 KET01 tablets 40 mg (pink) and 2 KET01 tablets 80 mg (white). Dose was taken once daily in the morning.

Duration of treatment:

Subjects received 240 mg KET01 as add-on treatment for a duration of 21 (\pm 2) days, starting at Visit 2b.

Subjects had to take 4 tablets, once daily in the morning together with a glass of water.

Arm title	Treatment - KET01-120
Arm description: KET01 120 mg once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial	
Arm type	Active comparator
Investigational medicinal product name	Ketamine hydrochloride (HCl)
Investigational medicinal product code	KET01
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

KET01 tablets 40 mg (pink), KET01 tablets 80 mg (white) and Placebo tablets matching KET01 tablets 40 mg (pink) and 80 mg (white) for oral administration.
Subjects took a total daily dose of 120 mg ketamine hydrochloride by 1 KET01 tablet 40 mg (pink), 1 KET01 tablet 80 mg (white), 1 Placebo tablet 40 mg (pink) and 1 Placebo tablet 80 mg (white). Dose was taken once daily in the morning.

Duration of treatment:

Subjects received 120 mg KET01 as add-on treatment for a duration of 21 (\pm 2) days, starting at Visit 2b.

Subjects had to take 4 tablets, once daily in the morning together with a glass of water.

Arm title	Treatment - Placebo
Arm description: Placebo once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

KET01 tablets 40 mg (pink), KET01 tablets 80 mg (white) and Placebo tablets matching KET01 tablets 40 mg (pink) and 80 mg (white) for oral administration.
Subjects took a total daily dose of 0 mg ketamine hydrochloride by 2 Placebo tablets 40 mg (pink) and 2

Placebo tablets 80 mg (white). Dose was taken once daily in the morning.

Duration of treatment:

Subjects received placebo as add-on treatment for a duration of 21 (± 2) days, starting at Visit 2b.

Subjects had to take 4 tablets, once daily in the morning together with a glass of water.

Number of subjects in period 2	Treatment - KET01-240	Treatment - KET01-120	Treatment - Placebo
Started	40	42	40
Completed	36	38	39
Not completed	4	4	1
Ineligibility/development of 1/mult. excl. crit.	1	1	-
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	1	2	-
Other	1	-	1
Lack of efficacy	-	1	-

Period 3

Period 3 title	Follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Follow-up - KET01-240

Arm description:

KET01 240 mg once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial

Arm type	Active comparator
Investigational medicinal product name	Ketamine hydrochloride (HCl)
Investigational medicinal product code	KET01
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

KET01 tablets 40 mg (pink), KET01 tablets 80 mg (white) and Placebo tablets matching KET01 tablets 40 mg (pink) and 80 mg (white) for oral administration.

Subjects took a total daily dose of 240 mg ketamine hydrochloride by 2 KET01 tablets 40 mg (pink) and 2 KET01 tablets 80 mg (white). Dose was taken once daily in the morning.

Duration of treatment:

Subjects received 240 mg KET01 as add-on treatment for a duration of 21 (\pm 2) days, starting at Visit 2b.

Subjects had to take 4 tablets, once daily in the morning together with a glass of water.

Arm title	Follow-up - KET01-120
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Arm description:

KET01 120 mg once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial

Arm type	Active comparator
Investigational medicinal product name	Ketamine hydrochloride (HCl)
Investigational medicinal product code	KET01
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

KET01 tablets 40 mg (pink), KET01 tablets 80 mg (white) and Placebo tablets matching KET01 tablets 40 mg (pink) and 80 mg (white) for oral administration.

Subjects took a total daily dose of 120 mg ketamine hydrochloride by 1 KET01 tablet 40 mg (pink), 1 KET01 tablet 80 mg (white), 1 Placebo tablet 40 mg (pink) and 1 Placebo tablet 80 mg (white). Dose was taken once daily in the morning.

Duration of treatment:

Subjects received 120 mg KET01 as add-on treatment for a duration of 21 (\pm 2) days, starting at Visit 2b.

Subjects had to take 4 tablets, once daily in the morning together with a glass of water.

Arm title	Follow-up - Placebo
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Arm description:

Placebo once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

KET01 tablets 40 mg (pink), KET01 tablets 80 mg (white) and Placebo tablets matching KET01 tablets 40 mg (pink) and 80 mg (white) for oral administration.

Subjects took a total daily dose of 0 mg ketamine hydrochloride by 2 Placebo tablets 40 mg (pink) and 2 Placebo tablets 80 mg (white). Dose was taken once daily in the morning.

Duration of treatment:

Subjects received placebo as add-on treatment for a duration of 21 (\pm 2) days, starting at Visit 2b.

Subjects had to take 4 tablets, once daily in the morning together with a glass of water.

Number of subjects in period 3 ^[2]	Follow-up - KET01- 240	Follow-up - KET01- 120	Follow-up - Placebo
Started	36	38	38
Completed	36	38	38

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: In total not only the subjects that completed the previous period but all 122 subjects started in the treatment period should be followed up and should complete a Follow-Up visit to document the development of score . In total 121 of 122 subjects did the Follow-Up visit. Due to technical issues only the 112 of 113 subjects, that completed the previous period and had a follow-up visit, could be stated here instead the 121 participating subjects.

Baseline characteristics

Reporting groups

Reporting group title	Baseline - KET01-240
Reporting group description:	
Defined due to technical issues: Subjects that were randomised to KET01-240 at Visit 2b. Visit 2a is part of preassignment screening period	
Reporting group title	Baseline - KET01-120
Reporting group description:	
Defined due to technical issues: Subjects that were randomised to KET01-120 at Visit 2b. Visit 2a is part of preassignment screening period	
Reporting group title	Baseline - Placebo
Reporting group description:	
Defined due to technical issues: Subjects that were randomised to Placebo at Visit 2b. Visit 2a is part of preassignment screening period	

Reporting group values	Baseline - KET01-240	Baseline - KET01-120	Baseline - Placebo
Number of subjects	40	42	40
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero	0	0	0
Preterm newborn- gestational age < 37 wk	0	0	0
Newborns (0-27days)	0	0	0
Infants and toddlers (28days – 23months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 year)	0	0	0
From 18 - 64 years	40	41	40
From 65 – 84 years	0	1	0
Over 85 years	0	0	0
Age Continuous			
Age Continuous Characteristic			
Units: years			
arithmetic mean	40.6	41.3	38.9
standard deviation	± 12.52	± 12.43	± 9.16
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	24	27	21
Male	16	15	19

Reporting group values	Total		
Number of subjects	122		
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero	0		

Preterm newborn- gestational age < 37 wk	0		
Newborns (0-27days)	0		
Infants and toddlers (28days – 23months)	0		
Children (2-11 years)	0		
Adolescents (12-17 year)	0		
From 18 - 64 years	121		
From 65 – 84 years	1		
Over 85 years	0		
Age Continuous			
Age Continuous Characteristic			
Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	72		
Male	50		

End points

End points reporting groups

Reporting group title	Baseline - KET01-240
Reporting group description: Defined due to technical issues: Subjects that were randomised to KET01-240 at Visit 2b. Visit 2a is part of preassignment screening period	
Reporting group title	Baseline - KET01-120
Reporting group description: Defined due to technical issues: Subjects that were randomised to KET01-120 at Visit 2b. Visit 2a is part of preassignment screening period	
Reporting group title	Baseline - Placebo
Reporting group description: Defined due to technical issues: Subjects that were randomised to Placebo at Visit 2b. Visit 2a is part of preassignment screening period	
Reporting group title	Treatment - KET01-240
Reporting group description: KET01 240 mg once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial	
Reporting group title	Treatment - KET01-120
Reporting group description: KET01 120 mg once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial	
Reporting group title	Treatment - Placebo
Reporting group description: Placebo once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial	
Reporting group title	Follow-up - KET01-240
Reporting group description: KET01 240 mg once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial	
Reporting group title	Follow-up - KET01-120
Reporting group description: KET01 120 mg once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial	
Reporting group title	Follow-up - Placebo
Reporting group description: Placebo once daily in addition to subject's current antidepressant treatment. Treatment with agreed ongoing antidepressant medication(s) had to be continued and to be kept at a stable dose throughout the trial	
Subject analysis set title	Treatment - KET01-240 x Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description: The safety set (SAF) was defined as all subjects who received at least one dose of IP.	
Subject analysis set title	Treatment - KET01-120 x Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description: The safety set (SAF) was defined as all subjects who received at least one dose of IP.	
Subject analysis set title	Treatment - Placebo x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety set (SAF) was defined as all subjects who received at least one dose of IP.

Subject analysis set title	Treatment - KET01-240 x Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set was defined as all subjects who received at least one dose of IP and who had at least one post-baseline assessment of primary efficacy measurement.

Subject analysis set title	Treatment - KET01-120 x Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set was defined as all subjects who received at least one dose of IP and who had at least one post-baseline assessment of primary efficacy measurement.

Subject analysis set title	Treatment - Placebo x Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set was defined as all subjects who received at least one dose of IP and who had at least one post-baseline assessment of primary efficacy measurement.

Subject analysis set title	Treatment - KET01-240 x Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol set (PPS) was defined as all subjects who were included into the FAS and had no major protocol deviations that could have an influence on the primary efficacy endpoint.

Subject analysis set title	Treatment - KET01-120 x Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol set (PPS) was defined as all subjects who were included into the FAS and had no major protocol deviations that could have an influence on the primary efficacy endpoint.

Subject analysis set title	Treatment - Placebo x Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol set (PPS) was defined as all subjects who were included into the FAS and had no major protocol deviations that could have an influence on the primary efficacy endpoint.

Primary: Change in MADRS total score

End point title	Change in MADRS total score
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End point description:

Change from baseline at Visit 2a to Visit 6 / early discontinuation visit (EDV) in MADRS total score.

End point type	Primary
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End point timeframe:

3 weeks

End point values	Treatment - KET01-240 x Full Analysis Set	Treatment - KET01-120 x Full Analysis Set	Treatment - Placebo x Full Analysis Set	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	40	42	40	
Units: [Score]				
number (standard deviation)				
Change	-13.4	-11.9	-11	

Statistical analyses

Statistical analysis title	MMRM, Full analysis set.
Statistical analysis description: mixed model for repeated measures (MMRM) with fixed effects of treatment, visit, visit and treatment interaction and baseline MADRS total score as a covariate as well as random effects of subject and country	
Comparison groups	Treatment - KET01-240 x Full Analysis Set v Treatment - Placebo x Full Analysis Set
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4125
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.21
upper limit	2.57
Variability estimate	Standard error of the mean
Dispersion value	2.215

Statistical analysis title	MMRM, Full analysis set.
Statistical analysis description: mixed model for repeated measures (MMRM) with fixed effects of treatment, visit, visit and treatment interaction and baseline MADRS total score as a covariate as well as random effects of subject and country	
Comparison groups	Treatment - KET01-120 x Full Analysis Set v Treatment - Placebo x Full Analysis Set
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8516
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.75
upper limit	3.93

Variability estimate	Standard error of the mean
Dispersion value	2.19

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs with the first onset or worsening after the first IP intake and not more than 14 days after the last IP intake were defined as TEAEs in this trial, the period of observation for the collection of AEs extends from informed consent given til final visit

Adverse event reporting additional description:

Only numbers of TEAEs are reported. Frequency threshold for reporting non-serious adverse event was set to 4%.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Treatment - KET01-240 x Safety Set
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Reporting group description:

Subjects in the Safety Set treated with KET01 240 mg

Reporting group title	Treatment - Placebo x Safety Set
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Reporting group description:

Subjects in the Safety Set treated with Placebo

Reporting group title	Treatment - KET01-120 x Safety Set
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Reporting group description:

Subjects in the Safety Set treated with KET01 120 mg

Serious adverse events	Treatment - KET01-240 x Safety Set	Treatment - Placebo x Safety Set	Treatment - KET01-120 x Safety Set
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	1 / 42 (2.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Non-serious adverse events	Treatment - KET01- 240 x Safety Set	Treatment - Placebo x Safety Set	Treatment - KET01- 120 x Safety Set
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 40 (50.00%)	13 / 40 (32.50%)	15 / 42 (35.71%)
Investigations			
Blood pressure diastolic increased			
subjects affected / exposed	0 / 40 (0.00%)	2 / 40 (5.00%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Inflammatory marker increased			
subjects affected / exposed	2 / 40 (5.00%)	0 / 40 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Hepatic enzyme increased			
subjects affected / exposed	4 / 40 (10.00%)	0 / 40 (0.00%)	1 / 42 (2.38%)
occurrences (all)	4	0	1
Heart rate increased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	2 / 42 (4.76%)
occurrences (all)	0	0	2
C-reactive protein increased			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	2 / 42 (4.76%)
occurrences (all)	0	1	2
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 40 (5.00%)	0 / 40 (0.00%)	1 / 42 (2.38%)
occurrences (all)	2	0	1
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	2 / 40 (5.00%)	1 / 40 (2.50%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
Headache			
subjects affected / exposed	4 / 40 (10.00%)	7 / 40 (17.50%)	5 / 42 (11.90%)
occurrences (all)	4	10	6
Dizziness			
subjects affected / exposed	7 / 40 (17.50%)	1 / 40 (2.50%)	2 / 42 (4.76%)
occurrences (all)	7	1	2
Somnolence			
subjects affected / exposed	1 / 40 (2.50%)	1 / 40 (2.50%)	2 / 42 (4.76%)
occurrences (all)	1	1	2

Paraesthesia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	0 / 40 (0.00%) 0	1 / 42 (2.38%) 1
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	1 / 40 (2.50%) 1	0 / 42 (0.00%) 0
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	0 / 40 (0.00%) 0	1 / 42 (2.38%) 1
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Dissociation subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0 2 / 40 (5.00%) 2 4 / 40 (10.00%) 4 2 / 40 (5.00%) 2	0 / 40 (0.00%) 0 0 / 40 (0.00%) 0 0 / 40 (0.00%) 0 0 / 40 (0.00%) 0	2 / 42 (4.76%) 2 1 / 42 (2.38%) 1 0 / 42 (0.00%) 0 0 / 42 (0.00%) 0
Infections and infestations Cystitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3 1 / 40 (2.50%) 1	0 / 40 (0.00%) 0 2 / 40 (5.00%) 2	1 / 42 (2.38%) 1 0 / 42 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported